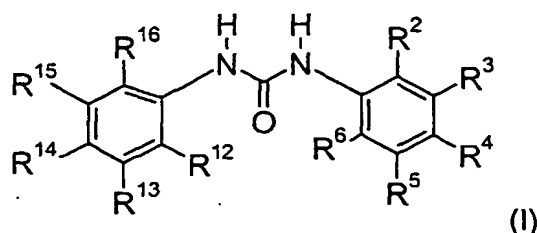


CLAIMS

- 5 1. The use of a compound of general formula I



or a pharmaceutically acceptable salt thereof

- 10 wherein R^2 represents tetrazolyl; and

- $R^3, R^4, R^5, R^6, R^{12}, R^{13}, R^{14}, R^{15}$, and R^{16} independently of each other represent hydrogen, halo, trifluoromethyl, nitro, alkyl, alkylcarbonyl, $-NR^aR^b$, $-NR^a-CO-R^b$, phenyl or heteroaryl;

- 15 which phenyl is optionally substituted with halo, trifluoromethyl, nitro, $-CO-NHR^c$, $-CO-O-R^c$ or $-CO-NR'R''$;

wherein R^c is hydrogen, alkyl, or phenyl;

R' and R'' independently of each other are hydrogen or alkyl; or

- 20 R' and R'' together with the nitrogen to which they are attached form a 5- to 7-membered heterocyclic ring, which ring may optionally comprise as a ring member, one oxygen atom, and/or one additional nitrogen atom, and/or one carbon-carbon double bond, and/or one carbon-nitrogen double bond;

and which heterocyclic ring may optionally be substituted with alkyl;

- 25 R^a and R^b independently of each other are hydrogen or alkyl; or

- R^{15} and R^{16} , or R^{14} and R^{15} together with the phenyl ring to which they are attached form a naphthyl ring or an indanyl ring; and $R^3, R^4, R^5, R^6, R^{12}$ and R^{13} and the remaining one of R^{14}, R^{15} and R^{16} are as defined above;

- 30 for the manufacture of a pharmaceutical composition for the treatment, prevention or alleviation of a disease or a disorder or a condition of a mammal, including a human, which disease, disorder or condition is responsive to inhibition of angiogenesis.

2. The use according to claim 1, wherein

- 35 R^3, R^5 , and R^6 represent hydrogen; and R^4 represents halo.

3. The use according to claim 1, wherein

R^3, R^5 , and R^6 represent hydrogen; and

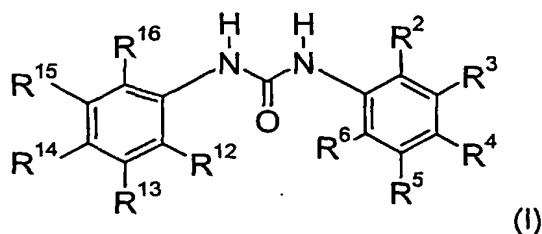
- 40 R^4 represents phenyl substituted with trifluoromethyl, nitro or $-CO-NHR^c$; wherein R^c is phenyl.

4. The use according to claim 1, wherein the compound is
N-4-Nitrophenyl-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-3,5-Di(trifluoromethyl)phenyl-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-3-Trifluoromethylphenyl-*N'*-[4-(3-nitrophenyl)-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
5 *N*-3-Trifluoromethylphenyl-*N'*-[4-(4-anilinocarbonylphenyl)-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-3-Trifluoromethylphenyl-*N'*-[4-(4-trifluoromethylphenyl)-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[4-bromo-2-(1-*H*-terazol-5-yl)-phenyl] urea;
N-(3-Trilfuoromethyl-phenyl)-*N'*-[4-phenyl-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
10 *N*-(3-Chloro-phenyl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[4-amino-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[4-acetylamino-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trilfuoromethyl-phenyl)-*N'*-[4-carbamoyl-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[4-(*N'*,*N'*-dimethylcarbamoyl)-2-(1-*H*-tetrazol-5-yl)-
15 phenyl] urea;
3'-(1-*H*-tetrazol-5-yl)-4'-[3-(3-trifluoromethyl-phenyl)-ureido]-biphenyl-4-carboxylic acid;
N-(Indan-5-yl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(Biphenyl-4-yl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(Biphenyl-3-yl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
20 *N*-(3-Acetyl-phenyl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(Biphenyl-3-yl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-[3-(Pyridin-3-yl)-phenyl]-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Bromo-phenyl)-*N'*-[4'-(4-methyl-piperazine-1-carbonyl)-3-(1-*H*-tetrazol-5-yl)-biphenyl-
4-yl] urea;
25 *N*-(3,5-Dichloro-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3,4-Dichloro-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(Naphthalen-1-yl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(2-Trifluoromethyl-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(2-Fluoro-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
30 *N*-(2-Ethyl-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
or a pharmaceutically acceptable salt thereof.

5. The use according to claim 1, wherein the disease, disorder or condition that is
responsive to inhibition of angiogenesis is selected from the group consisting of cancer,
35 prostate cancer, lung cancer, breast cancer, bladder cancer, renal cancer, colon cancer,
gastric cancer, pancreatic cancer, ovarian cancer, melanoma, hepatoma, sarcoma,
lymphoma, exudative macular degeneration, age-related macular degeneration,
retinopathy, diabetic retinopathy, proliferative diabetic retinopathy, diabetic macular edema
(DME), ischemic retinopathy, retinopathy of prematurity, neovascular glaucoma, corneal
40 neovascularization, rheumatoid arthritis, and psoriasis.

6. The use according to claim 1, wherein the compound is
N-4-Nitrophenyl-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-3,5-Di(trifluoromethyl)phenyl-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-3-Trifluoromethylphenyl-*N'*-[4-(3-nitrophenyl)-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
 5 *N*-3-Trifluoromethylphenyl-*N'*-[4-(4-anilinoacarbonylphenyl)-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-3-Trifluoromethylphenyl-*N'*-[4-(4-trifluoromethylphenyl)-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
 or a pharmaceutically acceptable salt thereof, and
 the treatment is an anti-metastatic treatment.
- 10 7. The use of a VRAC blocker or a pharmaceutically acceptable salt thereof for the
 manufacture of a pharmaceutical composition for the treatment, prevention or alleviation of
 age-related macular degeneration of a mammal, including a human.

8. The use according to 7, wherein the VRAC blocker is a compound of general
 15 formula I



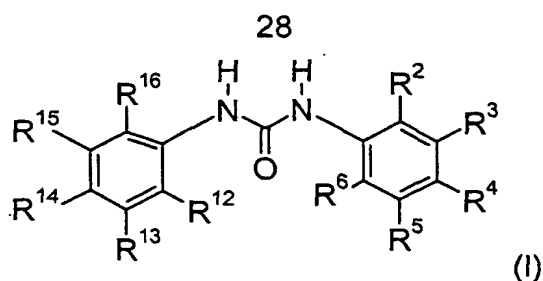
or a pharmaceutically acceptable salt thereof

- 20 wherein R² represents tetrazolyl; and

- R³, R⁴, R⁵, R⁶, R¹², R¹³, R¹⁴, R¹⁵, and R¹⁶ independently of each other represent hydrogen, halo, trifluoromethyl, nitro, alkyl, alkylcarbonyl, -NR^aR^b, -NR^a-CO-R^b, phenyl or heteroaryl;
 which phenyl is optionally substituted with halo, trifluoromethyl, nitro, -CO-NHR^c,
 25 -CO-O-R^c or -CO-NR^cR^c;
 wherein R^c is hydrogen, alkyl, or phenyl;
 R' and R'' independently of each other are hydrogen or alkyl; or
 R' and R'' together with the nitrogen to which they are attached form a 5- to 7-
 membered heterocyclic ring, which ring may optionally comprise as a ring member,
 30 one oxygen atom, and/or one additional nitrogen atom, and/or one carbon-carbon
 double bond, and/or one carbon-nitrogen double bond;
 and which heterocyclic ring may optionally be substituted with alkyl;
 R^a and R^b independently of each other are hydrogen or alkyl; or
- R¹⁵ and R¹⁶, or R¹⁴ and R¹⁵ together with the phenyl ring to which they are attached
 form a naphthyl ring or an indanyl ring; and R³, R⁴, R⁵, R⁶, R¹² and R¹³ and the
 35 remaining one of R¹⁴, R¹⁵ and R¹⁶ are as defined above.

9. The use according to claim 7, wherein the compound is
N-4-Nitrophenyl-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-3,5-Di(trifluoromethyl)phenyl-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-3-Trifluoromethylphenyl-*N'*-[4-(3-nitrophenyl)-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
 5 *N*-3-Trifluoromethylphenyl-*N'*-[4-(4-anilinocarbonylphenyl)-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-3-Trifluoromethylphenyl-*N'*-[4-(4-trifluoromethylphenyl)-2-(1-*H*-tetrazol-5-yl)phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[4-bromo-2-(1-*H*-terazol-5-yl)-phenyl] urea;
N-(3-Trilfuoromethyl-phenyl)-*N'*-[4-phenyl-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
 10 *N*-(3-Chloro-phenyl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[4-amino-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[4-acetylamino-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trilfuoromethyl-phenyl)-*N'*-[4-carbamoyl-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Trifluoromethyl-phenyl)-*N'*-[4-(*N''*,*N''*-dimethylcarbamoyl)-2-(1-*H*-tetrazol-5-yl)-
 15 phenyl] urea;
 3'-(1-*H*-tetrazol-5-yl)-4'-[3-(3-trifluoromethyl-phenyl)-ureido]-biphenyl-4-carboxylic acid;
N-(Indan-5-yl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(Biphenyl-4-yl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(Biphenyl-3-yl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
 20 *N*-(3-Acetyl-phenyl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(Biphenyl-3-yl)-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-[3-(Pyridin-3-yl)-phenyl]-*N'*-[2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3-Bromo-phenyl)-*N'*-[4'-(4-methyl-piperazine-1-carbonyl)-3-(1-*H*-tetrazol-5-yl)-biphenyl-
 4-yl] urea;
 25 *N*-(3,5-Dichloro-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(3,4-Dichloro-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(Naphthalen-1-yl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(2-Trifluoromethyl-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
N-(2-Fluoro-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
 30 *N*-(2-Ethyl-phenyl)-*N'*-[4-bromo-2-(1-*H*-tetrazol-5-yl)-phenyl] urea;
 or a pharmaceutically acceptable salt thereof.

10. A method of treatment, prevention or alleviation of a disease or a disorder or a
 condition of a living animal body, including a human, which disorder, disease or condition
 35 is responsive to inhibition of angiogenesis, comprising the step of administering to such a
 living animal body, including a human, in need thereof a therapeutically effective amount of
 a compound of general formula I



or a pharmaceutically acceptable salt thereof

wherein R^2 represents tetrazolyl;

- 5 • $R^3, R^4, R^5, R^6, R^{12}, R^{13}, R^{14}, R^{15}$, and R^{16} independently of each other represent hydrogen, halo, trifluoromethyl, nitro, alkyl, alkylcarbonyl, $-NR^aR^b$, $-NR^a-CO-R^b$, phenyl or heteroaryl;
 which phenyl is optionally substituted with halo, trifluoromethyl, nitro, $-CO-NHR^c$, $-CO-O-R^c$ or $-CO-NR'R''$;
 - 10 wherein R^c is hydrogen, alkyl, or phenyl;
 R' and R'' independently of each other are hydrogen or alkyl; or
 R' and R'' together with the nitrogen to which they are attached form a 5- to 7-membered heterocyclic ring, which ring may optionally comprise as a ring member,
 one oxygen atom, and/or one additional nitrogen atom, and/or one carbon-carbon
 15 double bond, and/or one carbon-nitrogen double bond;
 and which heterocyclic ring may optionally be substituted with alkyl;
 R^a and R^b independently of each other are hydrogen or alkyl; or
 - 20 • R^{15} and R^{16} , or R^{14} and R^{15} together with the phenyl ring to which they are attached form a naphthyl ring or an indanyl ring; and $R^3, R^4, R^5, R^6, R^{12}$ and R^{13} and the remaining one of R^{14}, R^{15} and R^{16} are as defined above.
11. A method of treatment, prevention or alleviation of age-related macular degeneration of a living animal body, including a human comprising the step of administering to
 25 such a living animal body, including a human, in need thereof a therapeutically effective amount of a VRAC blocker or a pharmaceutically acceptable salt thereof.